Artemisitene suppresses tumorigenesis by inducing DNA damage through deregulating c-Myc-topoisomerase pathway.

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Public Summary:
Cancer chemotherapeutic agents such as doxorubicin are DNA damage inducers that also kill normal cells, making them highly toxic to cancer patients. To improve the efficacy and safety of chemotherapy, it is important to develop new chemotherapeutic agents that selectively kill cancer cells. Here we demonstrate that artemisitene (ATT), a natural derivative of the antimalarial drug artemisinin, selectively induces DNA double-stranded breaks (DSBs) and apoptosis in various human cancer cells by suppressing the expression of topoisomerases in human cancer cells. ATT effectively kills human cancer cells without apparent cytotoxicity on normal human cells or mouse liver and kidney. We discovered that c-Myc induces the expression of topoisomerases to prevent accumulation of DNA damage in human cancer cells. ATT selectively destabilizes c-Myc in human cancer cells by promoting the ubiquitination of c-Myc through the specific induction of the c-Myc E3 ligase NEDD4. Therefore, ATT represents a promising new chemotherapeutic drug candidate that can eliminate human cancer cells with minimized cytotoxic effects on normal cells.

Scientific Abstract:
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